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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,363	11/15/2001	Richard C. Duke	3923-3	2524

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,363	DUKE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25, 29-33* is/are pending in the application.

4a) Of the above claim(s) *4-7,10 and 16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,9,11-15 and 29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application.

1. In the prior action, mailed on December 2, 2003, claims 1-3, 8, 9, and 11-15 were rejected, with claims 4-7, 10, and 16-28 withdrawn as to non-elected inventions. In the Response, filed on May 26, 2004, the Applicant amended claims 1 and 16(withdrawn); cancelled claims 26-28; and added new claims 29-33.

2. Currently, claims 1-25, and 29-33 are pending in the application, with claims 1-3, 8, 9, and 29-33 under consideration.

3. Because this action raises new grounds of rejection, it is made Non-Final.

Priority

4. **(Prior Objection-Maintained)** In the prior action, it was noted that application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). However, the application did contain such a reference. The Applicant has submitted the required reference. However, as this reference was submitted after the time period allotted in 37 CFR 1.78(a)(5), and as there has been no submission of the petition for unintentionally delayed claim to priority as required by 37 CFR 1.78(a)(6), the Applicant has still not met the conditions for priority to the provisional application 60/249,173 under 35 U.S.C. §119(e).

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. **(New Rejection)** Claims 1-3, 8, 9, 11-15, and 29-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on any therapeutic compositions comprising a dendritic cell, a yeast vehicle, and an antigen. Thus, the claimed compositions include embodiments wherein the dendritic cells which have incorporated the yeast vehicle and the antigen are inside a human being. Dendritic cells are known to take up antigens within an organism. See e.g., Sousa et al. J Exp Med 178: 509-19 (of record in the prior action). Thus, dendritic cells that have taken up yeast cells and other antigens may be found in nature. Because dendritic cells induce immune response to such antigens, they are inherently therapeutic in nature. The claims therefore read on non-statutory subject matter.

It is suggested that the claims be amended such that they read on compositions wherein the cells are - -isolated- -, thereby excluding embodiments wherein the composition may be found in nature.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. **(Prior Rejection- Maintained)** Claims 1, 2, 3, 8, 9, 11-15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions wherein the dendritic cells are loaded with either whole cell or spheroplast yeast vehicles and an antigen, does not reasonably provide enablement for therapeutic compositions wherein the dendritic cells is loaded with any yeast vehicle and an antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. These claims read on therapeutic compositions comprising a dendritic cell, a yeast vehicle, and an antigen. The Applicant has suggested that any form of yeast vehicle that can be used with an antigen in a dendritic cell vaccine or as an adjuvant may be used in the claimed composition. Page 10, lines 21-23. Thus, the claims read broadly on dendritic cell vaccines comprising an antigen and any yeast vehicle. The rejection is maintained and extended to new claims 29-33.

The claims were rejected on two grounds.

First, the claims were rejected for the scope of the yeast vehicles described in the claims. With reference to this ground of rejection, the office action asserted that the application was not enabled for compositions comprising any yeast vehicle, but only those comprising a yeast cell wall, or a yeast spherolplasts. The Applicant traverses this rejection on the basis that the yeast vehicles of the claimed invention need not necessarily provide an adjuvant effect, so long as the yeast particle has "the characteristic of being able to deliver antigens to the DCs in concentrated packages that can be avidly internalized." However, even if this is the case, the Applicant has still not enabled those in the art to practice the full scope of the claimed invention. Even with the alternative function, the claims still read on the use of any yeast vehicle, which can include any

yeast-derived particle. However, the application and the art recognize only a limited number of embodiments of yeast vehicles. Further, all of the examples in the application are directed to embodiments wherein the vehicle comprises a yeast particle comprising a cell wall. There are no examples of any subcellular particles (which includes individual yeast proteins and other constituent molecules) that may be used in the claimed composition. Nor is there any guidance towards particles that would be effective in the claimed compositions, or evidence that such particles would be effective.

In view of the breadth of the claims, and the limited guidance and examples provided by the application, the rejection that the claims exceed the scope of yeast vehicles for which the Applicant is enabled is maintained.

The second ground of rejection was that the Applicant had not provided an enabling description of the claimed inventions to the extent that they read on "therapeutic" compositions to any antigen or disease. The claims were also rejected because the Applicant has not demonstrated that the claimed compositions would have therapeutic effect against any antigenic source. The Applicant traverses the rejection on the grounds that "the specification does not require that the claimed composition actually cure or significantly reduce any or all symptoms of the disease, but rather that the compositions provide some therapeutic benefit, which can simply include elicitation of an immune response..." This argument is not found persuasive. First, the limitations set forth in the claims, rather than the embodiments described in the specification, determine the invention under examination. Even if the specification describes embodiments wherein the compositions merely induce an immune response, the claims require that the composition be a therapeutic composition. The art indicates that the term "therapeutic" requires

that some beneficial result. See e.g., definition of therapeutic in Stedman's Online Medical Dictionary, 27th Ed. Further, the portion of the specification cited by the Applicant (page 22, lines 15-35) does not indicate that an immune response alone is sufficient to induce a therapeutic effect, but that the immune response results in protection of the animal against the disease, or at least a reduction of the symptoms, occurrence, or severity of the disease. Thus, the claims require that the claimed compositions have some therapeutic effect. As the Applicant has not provided enabling support for claims drawn to compositions with a therapeutic effect against he full scope of pathogens and diseases falling within the claims. It is noted that the office action specifically indicates that the Applicant is enabled for immunogenic compositions. Thus, an amendment of the claims to read on immunogenic, rather than therapeutic, compositions would be enabled.

Claim Rejections - 35 USC § 102

9. **(Prior Rejection- Withdrawn)** Claims 1, 6, 11, 13, 14, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Sousa et al., J Exp Med 178(2): 509-19. The Applicant has amended the claims to require that the antigen is heterologous to the yeast cell. In view of this amendment , the rejection is amended.

Claim Rejections - 35 USC § 103

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. **(Prior Rejection- Withdrawn)** Claims 1-3, 8, 9, and 11-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Duke et al. (U.S. Patent 5,830,463- of record in the IDS of July 2002), in view of the teachings of Cohen et al. (U.S. Patent 6,187,307). In view of the arguments presented in the Response, the rejection is withdrawn.

12. **(New Rejection)** Claims 1-3, 8, 9, and 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Barbera-Guillem (U.S. Pub 2002/0155108) and Paglia et al. (J Exp Med, 183: 317-22) in view of Duke et al. (U.S. Patent 5,830,463). These claims read on therapeutic compositions comprising a dendritic cell (DC), a yeast vehicle, and at least one antigen. The term yeast vehicle is being interpreted as comprising a particle composed of materials from a yeast cell membrane. The particle may comprise the whole (intact or resealed) cell membrane, or may be, for example, a microparticle made from the sonication of the yeast membrane.

Barbera-Guillem teaches that dendritic cells loaded ex vivo with antigens are effective at inducing immune responses against target cells. Pages 1-2. The reference teaches that the administration of dendritic cells in combination with cells expressing the target antigen enables the combination to induce both $CD8^+$ and $CD4^+$ T-cell immune responses. Page 2, paragraph [0010], and page 5, paragraph [0034]. Additionally, Paglia teaches that dendritic cells pulsed with soluble antigen ex vivo are able to induce both types of immune responses. Page 317. The references therefore suggest the administration of antigens to dendritic cells such that both types of immune responses are induces, and teach that this may be achieved through the administration

of antigens to dendritic cells in vitro. The references do not however teach that yeast vehicles may be used for the delivery of such antigens.

Duke teaches a yeast vehicle useful in therapeutic compositions. Abstract. The reference further teaches that these particles are efficient vehicles for transporting antigens to cells, including dendritic cells. Column 13, lines 36-53. The reference further teaches that the particles are effective in stimulating both humoral and cell-mediated immunity. Abstract, and column 18, lines 30-33. Among the uses for the vehicle disclosed in the application is the delivery of the particles to cells, including dendritic cells. Columns 13-14. The reference further teaches that the delivery may be made ex vivo or in vitro, such that the particles can be absorbed by the cells, and the cells can then be returned to the animal from which they were isolated. Col. 19, lines 19-34. The reference teaches that such a method of delivery is useful in the induction of immune responses and in the treatment of tumors. Id. From these teachings, it would have been obvious to those in the art that the administration of the yeast vehicles with an antigen performs the same functions as the cells or soluble antigens in the Barbera-Guillem and Paglia references. Thus, the art demonstrates that the yeast vehicles are functional equivalents of the antigen delivery devices of the two later references. In view of these teachings, and the indication in the Duke reference that the yeast vehicles may be used to deliver antigens to dendritic cells, and that the delivery may be made in vitro or ex vivo, it would have been obvious to those in the art to make and use the claimed compositions.

It is noted that the Applicant asserts that the claimed compositions achieves unexpected results (increased immunogenic potency) than either DC exposed to antigens, or yeast vehicles plus antigen alone. However, there does not appear to be any evidence to support the assertion

that the claimed compositions are more potent that than the prior art DC vaccines. The examples of the present application do not appear to anywhere show a comparison of the claimed compositions to those such as are described in Paglia or Barbera-Guillem. In view of the lack of evidence of unexpected results over the closest prior art, the assertion of unexpected results is not found persuasive.

13. **(Prior Rejection- Withdrawn)** Claims 1, 2, 9, 13-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Layton et al. (Immunol 87:171-78) and Adams et al. (Intern Rev Immunol 11:133-41) in view of the teachings of Tomai et al. (U.S. Patent 6,558,951). In view of the arguments presented in the Response, the rejection is withdrawn.

14. **(Prior Rejection- Maintained)** Claims 1-3, 8, 9, and 11-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Duke in view of the teachings of Tomai. The claims have been described above, and the teachings of the identified references were described in the prior action. The Applicant traverses the rejection on three grounds. First, the Applicant argues that the two references do not teach all of the claim limitations. Second, the Applicant argues that there is no suggestion in the references to combine them. Finally, the Applicant asserts that the claimed compositions, even if prima facie obvious, achieve unexpected results. These arguments are not found persuasive. The rejection is therefore maintained against claims 1-3, 8, 9, and 11-15, and extended to new claims 29-33.

The first argument is not found persuasive. While the Applicant does not state what limitations are not taught by the combination, the argument appears to be that neither one of the

references teaches each of the three elements. This argument is not persuasive because, while the Examiner agrees that neither one of the references teaches all of the claimed limitations, the rejection is based on the combination of the references and not each independently. It is established law that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Thus, the Applicant's arguments that the references do not individually teach the claimed methods are not found persuasive.

The second ground of rejection is that the there is not suggestion in the references to combine them. The Applicant asserts that the Examiner indicates that the teachings of Duke and Tomai are equivalent, and would cause one of ordinary skill in the art to combine them. However, this is not accurate. Rather, the references were described in the prior action as complementary. The Duke reference teaches the use of yeast vehicles to deliver antigens to DC cells, and the Tomai reference teaches the therapeutic administration of activated DC cells. In particular, Duke teaches that DC cells may be beneficially exposed to antigens through use of the yeast vehicles such that the cells will induce both cell-mediated responses it is noted that, while the reference indicates that adjuvants may not be required (col. 2, lines 35-45), the patent also teaches (e.g. claim 11) that adjuvants may be used in combination with the yeast vehicles.

Tomai teaches that, after the cells have been exposed to an antigen, they may be further exposed to additional immune response modifiers to further increase the immune potency of the cells. Tomai, columns 15, lines 23-55. Thus, from these teachings it would have been obvious to those in the art to use the yeast vehicles of Duke to deliver the antigens to the DCs used in the

methods of generating an immune response disclosed in Tomai. There is no indication in the references that the methods of the two references are distinct (in that they cannot be combined) as suggested by the Applicant. The Applicant's second argument in traversal is therefore not found persuasive.

Finally, the Applicant again asserts unexpected results. However, as indicated above, the Applicant has provided no evidence of such results in relation to the closest prior art, the use of antigen activated DC compositions. For these reasons, and the reasons above, the rejection is maintained.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 9/7/04
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